IV. The claimed invention is novel

Novelty over Kalled et al.

The Examiner has rejected claims 3-5 under 35 U.S.C. § 102(b) over Kalled et al. (WO 98/39026) on the assertion that Kalled et al. teach methods of treating ITP with anti-CD40L and that it would have been inherent in treating ITP patients with anti-CD40L antibodies to prevent the onset of ITP and when the candidate's immune response to platelet begins in that such ITP patients would have been treated during remissions or in combination with standard therapies.

The present invention is directed towards a "method of preventing onset of idiopathic thrombocytopenic purpura (ITP), comprising administering to a candidate for the prevention a substance inhibiting interaction between gp39 on a T cell surface and CD40 on an antigen-presenting cell surface in an amount effective to prevent onset of ITP, said gp39 being a receptor which mediates a contact-dependent helper-effector function," as recited in claim 3. Amended claim 5 specifies that the administration of the substance is initiated when there is not a decrease in the candidate's platelet count. This is illustrated within the Examples on pages 11 to 14, where the administration of the "substance" to the (NZW X BXSB) F_1 mice was performed beginning at 5 weeks of age.

Kalled et al. disclose administering anti-CD40L antibodies to the (SWR X NZB) F_1 mice beginning at 4.5 months of age when the disease state is in its progression (*see* Figures and Experiments (pages 13-16) , not at the onset as required by the presently claimed invention. Therefore, Kalled et al. do not anticipate the presently claimed invention since the reference does not teach prevention of the onset of ITP as required in the presently claimed invention.

Thus, the cited reference cannot anticipate the claims and Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b).

Novelty over Black et al.

The Examiner has rejected claims 3-5 under 35 U.S.C. § 102(e) over Black et al. (USP 6,001,358) on the assertion that Black et al. teach methods of treating ITP with anti-CD40L and that it would have been inherent in treating ITP patients with anti-CD40L antibodies to prevent the onset of ITP and when the candidate's immune response to platelet begins in that such ITP patients would have been treated during remissions or in combination with standard therapies.

As stated above, the presently claimed invention relates to a method for preventing the onset of ITP by administration of a substance which inhibits the interaction between gp39 on a T cell surface and CD40 on an antigen-presenting cell surface and that the administration occurs when there is not a decrease in the candidate's platelet count. This is demonstrated within the Examples and Figures of the present invention.

Black et al. disclose a humanized antibody and pharmaceutical composition containing the humanized antibody and possible disease conditions in which to administer the humanized antibody and/or pharmaceutical composition, including ITP. Aside from a generalized comments, Black et al. do not discuss the prevention of the onset of a disease and/or at what stage such prevention would occur as required by the presently claimed invention.

Thus, Black et al. does not anticipate the presently-claimed invention and Applicants respectfully request withdrawal of the rejection to the claims under 35 U.S.C. § 102(e).

Novelty over Lederman et al.

The Examiner has rejected claims 3-5 under 35 U.S.C. § 102(e) over Lederman et al. (USP 5,993,816) on the assertion that Lederman et al. teach methods of treating ITP with 5C8-specific antibodies and that it would have been inherent in treating ITP patients with anti-CD40L antibodies to prevent the onset of ITP and when the candidate's immune response to platelet begins in that such ITP patients would have been treated during remissions or in combination with standard therapies.

The presently claimed invention is directed towards a "method of preventing the onset of...(ITP)...candidate for prevention..." as recited in claim 3. This is further characterize in amended claim 5 where it states that the administration occurs when the candidate's platelet count does not decrease. Lederman et al. is silent with regards to preventing the onset of ITP and does not disclose the administration of "...a substance inhibiting interaction between gp39 on a T cell surface and CD40 on an antigen-presenting cell surface" for preventing the onset of an autoimmune disease (ITP). In addition, Lederman et al. fails to disclose any substantive data illustrating the effectiveness of the anti-5C8 antibodies in the prevention of such an autoimmune disease. In view of the failure to disclose prevention of the onset of an autoimmune disease, examples and/or data supporting the use of the disclosed anti-5C8 antibodies, the rejection for anticipation fails. Thus, Lederman et al. does not anticipate the presently-claimed invention and Applicants respectfully request withdrawal of the rejection to claims 3-5 under 35 U.S.C. § 102(e).

V. The claimed invention is non-obvious

The Examiner rejected the claims under 35 U.S.C. § 103(a) on the assertion that the following cited references anticipate the invention as claimed. Specifically, the Examiner asserts that the combination of Kalled et al. and/or Black et al. and/or Lederman et al. in view of either one of : Nemoto et al. (Br. J. Haematol. 91:691-696, 1995), Medical Letter on Drugs and Therapeutics (39:6-8, 1996), or Williams et al. (Br. J. Haematol. 101:779-782, 1998) make obvious the presently claimed invention.

In order for a combination of references to render a claim obvious, the combination of references must teach or suggest each of the elements of the claimed invention and must also provide the motivation to combine these elements to create the claimed invention. *In re Fine*, 5 U.S.P.Q.2d 1597 (Fed. Cir. 1988), *In re Rouffet*, 47 U.S.P.Q.2d 1453, 1456 (Fed. Cir. 1998) and *In re Geiger*, 2 U.S.P.Q.2d 1276 (Fed. Cir. 1987) *In re Dembiczak* (175 F.3d 994, 50 U.S.P.Q.2d 1614 (Fed. Cir. 1999) As discussed below, the cited combination of references does not suggest all of the elements of the claimed invention, nor does the cited combination of references provide a motivation to combine the elements to create the claimed invention.

As discussed above, the cited references of Kalled et al., Black et al., and Lederman et al. do not teach the presently claimed invention. There is no disclosure within the references either alone or in combination with each other to prevent the onset of ITP by administering a substance which inhibits the interaction between gp39 on a T cell surface and CD40 on an antigen-presenting cell surface in such a way to convey to one of skill in the art that such administration would be effective in prevention of ITP disease state. Nor is there a disclosure within any of the cited references to administer the substance at a stage when there is not a decrease in the platelet count of the candidate as required by the presently claimed invention.

The presently claimed invention describes in the Examples and the Figures the administration of the substance at a stage before the ITP disease state has developed. As described in Figure 2, the mice were administered the MR1 at five weeks of age, and the test group retained stability within their platelet count for the 12-week trial period. Thus, the Applicants described objective evidence of success of the presently claimed in their disclosure.

Of the cited references, only Kalled et al. exemplify the administration of their anti-CD40L to autoimmune compromised mice. However, this administration was performed at 4.5 months (~22 weeks). Therefore, the above cited combination of references offered no reasonable expectation of success in the prevention of the onset of ITP since the references are silent as to how or when such administration of an anti-gp39 antibody would effectively prevent the onset of ITP.

The Examiner further mentions Nemoto et al., Medical Letter on Drugs and Therapeutics and/or Williams et al. in the cited combination of references. However, as discussed above, the cited combination of Kalled et al., Black et al., and/or Lederman et al. does not make obvious the presently claimed invention. These additional cited references do not make up the deficiencies in Kalled et al., Black et al., and/or Lederman et al. since they do not teach or suggest the prevention of ITP by administering a substance (e.g. anti-gp39 antibody) which inhibits the interaction between gp39 on a T cell surface and CD40 on an antigen-presenting cell surface, nor is there any teaching or suggesting of preventing ITP at a

stage where the candidate's platelet count does not decrease as required by the presently claimed invention. Therefore, the above cited combination of references does not teach or suggest all of the claimed elements of the present invention as required by M.P.E.P. 2143.

In view of the above remarks, Applicants respectfully request withdrawal of the rejection to claims 3-5 under 35 U.S.C. § 103(a).

IV. Conclusion

Claim 5 has been amended and the specification has been amended to clarify the Title of the Invention and correct a minor informality. These changes made to the specification and claims by the current amendment, including insertions and **[deletions]**, are shown on an attached sheet entitled **VERSION WITH MARKINGS TO SHOW CHANGES MADE**, which follows the signature page of this amendment.

Should any issues remain that may be addressed by a phone conversation, the Examiner is invited to contact the undersigned at the phone number listed below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 27 December 2002

By: _____

Megan M. McCoy
Registration No. 51,345
Agent of Record
Customer No. 20,995
(805) 547-5581

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification

The Title of the Invention has been amended as follows:

[AGENT FOR]PREVENT**[ING]**ION OF IDIOPATHIC THROMBOCYTOPENIC PURPURA USING A gp39 ANTAGONIST

On page 8, the first full paragraph has been amended as follows:

The agent for preventing ITP of the present invention can be administered to a patient expected to develop ITP (including ITP patients in remission owing to administration of a steroid drug or the like) to prevent an onset (as well as exacerbation) of **[IPT]**ITP.

In the claims

5. **(Amended)** The method according to Claim 3, wherein the administration of the substance is initiated when the **[candidate's immune response to]**number of platelets **[begins]**in the candidate does not decrease.